REMARKS

The following remarks are offered in complete response to the Official Action/Restriction and Election of Species Requirement dated June 26, 2006. In light of these remarks, reconsideration of the requirements and examination of all of the claimed subject matter on the merits are respectfully requested.

The acknowledgements of the claim for foreign priority and receipt of the certified copy of the priority document are noted, with appreciation.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, 33 and 35-60 are now in this application.

Claims 2-8, 32 and 34 have been cancelled by the foregoing amendment. Claims 12, 15, 18-20, 22, 23, 26, 30 and 31 were previously cancelled.

Claims 1, 21, 24, 25, 27-29, 33 and 35-42 have been amended. Claims 1, 24, 25 and 27-29 have been amended to remove the phrase "or precursor thereof", thereby restricting the claims to hydrolase polypeptides having amidase activity and not precursors thereof. Claims 1, 24, 25, 27, 28 and 29 have also been amended to restrict the hydrolase polypeptide having amidase activity to the members of the listed Markush group. Support for this amendment is found in paragraph [0022] of the specification. Claim 21 has been amended to delete the phrase "or a mixture thereof" and to add the word "or" before the last member of the group of agents. Claims 24, 25, 27-29 have been amended to delete the phrase " and/or for promoting cell renewal in the skin and/or for promoting cell proliferation in the skin and/or for promoting cell differentiation in the skin". Claims 33 and 35-42 have been amended to restrict the hydrolase polypeptide having amidase activity to aspartylglucosaminidase (AGA), by removing Markush group language and deleting the other members of the Markush group. Applicants reserve the right to pursue

claims drawn to methods of using hydrolase polypeptides having amidase activity no longer encompassed by the claims in a separate application.

Claims 43-60 have been added. Claims 43-60 parallel Claims 27, 1, 16, 17, 21, 24, 25, 28, 29, 33, 35, 36, 37, 38, 39, 40, 41, 42, respectively, with the restriction that the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate. Support for this amendment is found at least in paragraph [0050] of the specification. No new matter has been added.

All of the claims now in the application read on the elected aspartylglucosaminidase (AGA) species and the elected α-hydroxy acid species. At least Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27, 33, 35-40, 43-49 and 52-58 read on the elected xerosis species.

The currently amended claims are divided into four groups.

Group 1 is the broadest group, consisting of Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25 and 27-29. These claims require applying (i) at least one hydrolase polypeptide having amidase activity selected from the group consisting of aspartylglucosaminidase (AGA), glutaminase, amidase, urease, aminoacylase, aspartoacylase, ceramidase, peptidyl-glutaminase, formamidase and pentanamidase, and (ii) at least one activator of the at least one hydrolase polypeptide. Support for the listed amidases is found in paragraph [0022] of the specification.

Group 2 is a narrower group than Group 1, and consists of Claims 33 and 35-42. These claims require that the at least one hydrolase polypeptide having amidase activity is aspartylglucosaminidase (AGA). The claims also require at least one activator of aspartylglucosaminidase (AGA) as defined in Group 1.

Group 3 is a narrower group than Group 1, and consists of Claims 43-51. These claims require that the at least one hydrolase polypeptide having amidase activity is selected from the list of amidases in Group 1 and limits the at least one activator to sodium dodecyl sulfate or sodium lauryl ether sulfate. Support for these activators is found in paragraph [0050] of the specification.

Group 4 is the narrowest group and consists of Claims 52-60. These claims require that the at least one hydrolase polypeptide having amidase activity is aspartylglucosaminidase (AGA). These claims also require that the at least one activator of aspartylglucosaminidase (AGA) is sodium dodecyl sulfate or sodium lauryl ether sulfate.

35 U.S.C. §112 first paragraph written description rejections

Claims 1-11, 13, 14, 16, 17, 21, 24, 25, 27-29 and 32 have been rejected under 35 U.S.C. §112, first paragraph, as purportedly failing to comply with the written description requirement. The Examiner alleges that the claims contain subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner has indicated that the Applicant has not identified which of the numerous hydrolase polypeptides having amidase activity, or precursors thereof, have the required effects as recited in the preamble of the claims.

Claims 1, 24, 25 and 27-29 have been amended to restrict the hydrolase polypeptide having amidase activity to the members of the group consisting of aspartylglucoamidase (AGA), glutaminase, amidase, urease, aminoacylase, aspartoacylase, ceramidase, peptidyl-glutaminase, formamidase and

pentanamidase. This is the broadest definition of the hydrolase polypeptide now set forth in the claims. Claims 2-8 and 32 have been cancelled. Claims 9-11, 13, 14, 16, 17 and 21 depend from Claim 1. Claims 1, 24, 25 and 27-29 have been amended to remove the phrase "or precursor thereof", thereby restricting the claims to the named hydrolase polypeptides having amidase activity and not precursors thereof.

The Examiner has indicated in the Office Action that there is written description for aspartylglucosaminidase (AGA). Therefore Claims 33 and 35-42 (Group 2) and Claims 52-60 (Group 4) without question convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention with respect to hydrolase polypeptide having amidase activity because they provide the identity of this specific hydrolase polypeptide having amidase activity.

Claims 1, 9, 10, 11, 13, 14, 16, 17, 21, 24, 25 and 27-29 (Group 1) and Claims 33 and 35-42 (Group 3) restrict the hydrolase polypeptide having amidase activity to the members of the group consisting of aspartylglucoamidase (AGA), glutaminase, amidase, urease, aminoacylase, aspartolacylase, ceramidase, peptidyl-glutaminase, formamidase and pentanamidase. Paragraph [0022] of the specification describes each of the listed hydrolase polypeptide having amidase activity along with aspartylglucoaminidase (AGA), which the Examiner has indicated is enabled, as specific examples of compounds of the family of hydrolases with the requisite enzymatic activity. These claims are therefore convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention with respect to these specific hydrolase polypeptides having amidase activity because they specifically identify these hydrolase polypeptides

having amidase activity and teach that they can be used in place of AGA (which is described in greater detail as representative of the group). There can no longer be any question as to written descriptions, for the specification clearly indicates to one of ordinary skill that the inventors had possession of the claimed invention with request to these ten hydrolases.

The Examiner also indicates that the specification only indicates sodium dodecyl sulphate (SDS) as an activator of a hydrolase polypeptide having amidase activity and does not describe any other compounds appropriate to activating the poypeptide. The Examiner is incorrect, first because paragraph [0050] of the specification provides examples of the activator being sodium dodecyl sulfate (SDS) or sodium lauryl ether sulfate, which are two distinct compounds. Moreover, paragraph [0047] of the specification provides a specific definition of an activator as:

> The expression "activator" is understood to mean either a product, or a set of products, capable of stimulating the activity of the said polypeptide, for example of increasing the rate of the enzymatic reaction, measured by the increase in the quantity of substrates digested per unit of time during the bringing of the AGA polypeptide into contact with the activator.

This conveys to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention with respect to the activator. Newly added claims 43-60 require that activator is sodium dodecyl sulfate or sodium lauryl ether sulfate. Paragraph [0050] of the specification provides sodium dodecyl sulfate and sodium lauryl ether sulfate as examples of activators.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25 and 27-29 (Group 1) and Claims 33 and 35-42 (group 2) require at least one activator. By providing the definition of an activator in paragraph [0047] of the specification, the Applicant has conveyed to one skilled in the relevant art that the inventors, at the time the application was filed, had

possession of the claimed invention with respect to the activators because they provide both a specific definition of an activator which provides the criteria that the skilled person would use to readily identify a suitable activator and the identities of two specific activators which can be employed.

Claims 43-51 (Group 3) and Claims 52-60 (Group 4) require that the at least one activator of the aminidase is sodium dodecyl sulfate or sodium lauryl ether sulfate. Support for these specific activators is found in paragraph [0050] of the specification. Therefore Claims 43-51 (Group 3) and Claims 52-60 (Group 4) without question convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention with respect to the activators because they provide a specific list of activators.

For at least the reasons given above, all claims now in the application are believed to be free of the record written description rejection.

35 U.S.C. §112 second paragraph rejections

Claims 3-6, 21 and 33-42 have been rejected under 35 U.S.C. §112, second paragraph, as purportedly being indefinite for failing to particularly point out and distinctly claim the subject matter which that applicant regards as the invention.

Claims 3-6 have been canceled and therefore rejection of these claims are moot.

The Examiner has indicated that Claims 21 and 38 are rendered indefinite by the recitation "or mixture thereof" since it appears that the claim requires a composition comprising all the ingredients recited prior to "or mixture thereof," and therefore renders "or mixture thereof" redundant. In light of the fact that "at least one" allows for the presence of one or more of the listed agents, the "or mixture

thereof" can be considered redundant. Therefore, Claim 21 has been amended to delete the phrase "or mixture thereof". Claim 38 depends from Claim 21. Therefore this rejection of Claims 21 and 38 are moot.

Claims 33-42 are considered indefinite by the Examiner by the recitation "aspartyglucosaminidase AGA" since AGA is an abbreviation of "aspartyglucosaminidase". All of the claims now shown that AGA is only an abbreviation of the term aspartylglucosaminidase by placing AGA in parenthesis, i.e. (AGA).

Claim 34 has been cancelled and therefore rejection of this claim is moot.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25 and 27-29 (Group 1) are not indefinite because the claims require applying (i) at least one hydrolase polypeptide having amidase activity selected from a group of specific hydrolase polypeptides and (ii) at least one activator of the at least one hydrolase polypeptide, where a specific definition of the activator has been provided in the specification.

Claims 33 and 35-42 (Group 2) are not indefinite because the claims require applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity, and (ii) at least one activator of aspartylglucosaminidase (AGA), where a specific definition of the activator has been provided in the specification.

Claims 43-51 (Group 3) are not indefinite because the claims require applying (i) at least one hydrolase polypeptide having amidase activity, selected from a group of specific hydrolase polypeptides and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate.

Claims 52-60 (Group 4) are not indefinite because the claims require applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase

activity and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate.

For at least the reasons given above, all of the claims now in the application are free of the record 35 U.S.C. § 112, second paragraph, rejection.

35 U.S.C. §102 prior art rejections

Claims 1, 7, 8, 16, 24, 25, 27-29 and 32 have been rejected under 35 U.S.C. §102(a) and 35 U.S.C. §102(e) as being anticipated by Meyers (US 2002/0038014).

Claims 1, 16, 24, 25, 27-29 remain in the instant application. Claims 7, 8 and 32 have been cancelled and therefore rejection of these claims are moot.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (MPEP 2131).

Meyers teaches novel asparaginases, referred to as "26443" and "46873", that are nucleic acid and protein molecules. Meyers teaches that these novel proteins can be therapeutic agents for controlling one or more of cellular proliferative and/or differentiative disorders, disorders associated with bone metabolism, immune disorders, hematopoietic disorders, cardiovascular disorders, liver disorders, viral diseases, pain or metabolic disorders. Examples of cellular proliferative and/or differentiative disorders include cancer, e.g., carcinoma, sarcoma, metastatic disorders or hematopoietic neoplastic disorders, e.g., leukemias. Meyers also teaches:

> The nucleic acid and polypeptides, fragments thereof, as well as anti-26443 or 46873 antibodies (also referred to herein as "active compounds") of the invention can be incorporated into pharmaceutical compositions. [0332]

Meyers further teaches:

> A pharmaceutical composition is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, and rectal administration. [0332]

Meyers also teaches:

> Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. [0332] (Note: underlining added by Applicant in this response to point out distinction needing emphasis as described below.)

The Examiner has misunderstood the teaching of Meyers by stating Meyers teaches that:

> "Additionally, the pharmaceutical compositions may include "citrates or phosphates and agents for the adjustment of tonicity" and agents for pH adjustment (page 29, paragraph 0333).

As stated by Meyers in paragraph [0333], the pharmaceutical compositions that may include "citrates or phosphates and agents for the adjustment of tonicity" and agents for pH adjustment are specifically for solutions or suspensions used for parenteral, intradermal, or subcutaneous application. Meyers does not teach the use of the materials in transdermal (topical) applications.

Claim 27 is the independent claim from which Claims 1, 16, 24, 25, 28 and 29 depend. Claim 27 is directed towards a regime or regimen for promoting desquamation of the skin and/or for promoting hydration of the skin of an individual in need of such treatment, comprising topically applying thereon thus effective

amounts of (i) at least one hydrolase polypeptide having amidase activity selected from the group consisting of aspartylglucosamidase (AGA), glutaminase, amidase, urease, aminoacylase, aspartoacylase, ceramidase, peptidyl-glutaminase, formamidase and pentanamidase, and (ii) at least one activator of said at least one hydrolase polypeptide.

Claim 27 of the instant application requires at least one hydrolase polypeptide having amidase activity selected from the group consisting of aspartylglucosaminidase (AGA), glutaminase, amidase, urease, aminoacylase, aspartoacylase, ceramidase, peptidyl-glutaminase, formamidase and pentanamidase. Meyers does not use any of these specific known hydrolase polypeptides having amidase activity.

Claim 27 of the instant application also requires at least one activator of said at least one hydrolase polypeptide. An activator is defined in paragraph [0047] of the specification of the instant application as "a product, or a set of products, capable of stimulating the activity of said polypeptide". Meyers does not use an activator for one of the specific hydrolase polypeptides having amidase activity as required in the claim.

Therefore the instant claims are not anticipated by Meyers and these rejections should be withdrawn.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25 and 27-29 (Group 1) are not anticipated by Meyers because the claims require applying: (i) at least one hydrolase polypeptide having amidase activity, selected from a group of specific hydrolase polypeptides listed within a Markush group, where the listed group was not taught by Meyers, and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator was not taught by Meyers.

Claims 33 and 35-42 (Group 2) are not anticipated by Meyers because the claims require applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity, and use of AGA was not taught by Meyers, and (ii) at least one activator of aspartylglucosaminidase (AGA), where use of an activator of AGA was not taught by Meyers.

Claims 43-51 (Group 3) are not anticipated by Meyers because the claims require applying (i) at least one hydrolase polypeptide having amidase activity, selected from a group of specific hydrolase polypeptides listed within a Markush group, where the members of the listed group were not taught by Meyer, and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate, where use of these activators was not taught by Meyers.

Claims 52-60 (Group 4) are not anticipated by Meyers because the claims require applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity, where the use of AGA was not taught by Meyers and (ii) the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate, where use of these activators of AGA was not taught by Meyers.

Further with respect to Meyers and all of the present claims, a method for treating cancer by inducing cell death does not inherently anticipate the present method for promoting desquamation of the skin and/or for promoting hydration of the skin. It is not correct to hold there is inherency. In addition to the difference in the hydrolase polypeptide, the method is applied to a different population. The individual in need of skin disquamation or hydration of applicants' claims is a healthy person or one having a desquamation problem. The person treated by Meyers is a cancer patient. This is an important distinction which means applicants' method is clearly

not anticipated by the method of Meyers. The method of Meyers is for treating cancer; Meyers does not put the skilled person in possession of a method of hydrating skin or promoting skin desquamation.

Claims 1-3, 7, 8, 16, 24, 25, 27-29, 32-36 and 39-42 have been rejected under 35 U.S.C. §102(e) as being anticipated by Rudolph-Owen et al. (WO 03/038113).

Claims 1, 16, 24, 25, 27-29, 33, 35, 36 and 39-42 remain in the instant application. Claims 2, 3, 7, 8, 32 and 34 have been cancelled and therefore rejection of these claims are moot.

Rudolph-Owen et al. teach that the expression of the 25943 gene is a polypeptide, referred to as "25943", that is a glycosylasparaginase. Rudolph-Owen et al. teach that 25943 can be used for the treatment of cellular proliferation disorders. Examples of cellular proliferation disorders include breast cancer, ovarian cancer, lung cancer, and/or colon cancer. Rudolph-Owen et al. also teach:

> The agents which modulate 25943 activity can be administered to a subject using pharmaceutical compositions suitable for such administration. [page 44 lines 33-34]

Rudolph-Owen et al. further teaches:

> A pharmaceutical composition used in the therapeutic methods of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, and rectal administration. [page 45 lines 10-13]

Rudolph-Owen et al. also teach:

> Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite;

> chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. [page 45 lines 13-22]
> (Note: underlining added by Applicant in this response to point out distinction needing emphasis as described below.)

The Examiner has misunderstood the teaching of Rudolph-Owen et al. by stating Rudolph-Owen et al. teaches:

> "citrates or phosphates and agents for the adjustment of tonicity" as well as acids or bases for pH adjustment may be used in the pharmaceutical composition (page 45, lines 19-21).

As stated by Rudolph-Owen et al. on page 45 lines 13-21, the pharmaceutical compositions that may include "citrates or phosphates and agents for the adjustment of tonicity" and agents for pH adjustment are specifically for solutions or suspensions used for parenteral, intradermal, or subcutaneous application. Rudolph-Owen et al. does not teach the use of the materials in transdermal (topical) applications.

Claim 27 is the independent claim from which Claims 1, 16, 24, 25, 28, 29 33, 35, 36 and 39-42 depend.

Claim 27 of the instant application requires at least one hydrolase polypeptide having amidase activity selected from the group consisting of aspartylglucoamidase (AGA), glutaminase, amidase, urease, aminoacylase, aspartoacylase, ceramidase, peptidyl-glutaminase, formamidase and pentanamidase. Rudolph-Owen et al. does not use any of these specific hydrolase polypeptide having amidase activity, but rather uses a glycosylasparaginase.

Claim 27 of the instant application also requires at least one activator of said at least one hydrolase polypeptide. An activator is defined in paragraph [0047] of the specification of the instant application as "a product, or a set of products, capable of

stimulating the activity of said polypeptide". Rudolph-Owen et al. does not use an activator for one of the specific hydrolase polypeptides having amidase activity as required in the claim.

Therefore the instant claims are not anticipated by Rudolph-Owen et al. and these rejections should be withdrawn.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25 and 27-29 (Group 1) are not anticipated by Rudolph-Owen et al. because the claims require applying: (i) at least one hydrolase polypeptide having amidase activity, selected from group of specific hydrolase polypeptides listed as members of a Markush group, where the listed group was not taught by Rudolph-Owen et al., and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator was not taught by Rudolph-Owen et al..

Claims 33 and 35-42 (Group 2) are not anticipated by Rudolph-Owen et al. because the claims require applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity, and use of AGA was not taught by Rudolph-Owen et al., and (ii) at least one activator of aspartylglucosaminidase (AGA), where use of an activator of AGA was not taught by Rudolph-Owen et al..

Claims 43-51 (Group 3) are not anticipated by Rudolph-Owen et al. because the claims require applying (i) at least one hydrolase polypeptide having amidase activity, selected from a group of specific hydrolase polypeptides listed as members of a Markush group, where the listed group was not taught by Rudolph-Owen et al., and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate, where use of these activators was not taught by Rudolph-Owen et al.

Claims 52-60 (Group 4) are not anticipated by Rudolph-Owen et al. because the claims require applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity, where the use of AGA was not taught by Rudolph-Owen et al. and (ii) the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate, where use of these activators of AGA was not taught by Rudolph-Owen et al.

Further with respect to Rudolph-Owen et al. and all of the present claims, a method for treating cancer by inducing cell proliferation does not inherently anticipate the present method for promoting desquamation of the skin and/or for promoting hydration of the skin. It is not correct to hold there is inherency. In addition to the difference in the hydrolase polypeptide, the method is applied to a different population. The individual in need of skin disquamation or hydration of applicants' claims is a healthy person or one having a desquamation problem. The person treated by Rudolph-Owen et al. is a cancer patient. This is an important distinction which means applicants' method is clearly not anticipated by Rudolph-Owen et al. method. Rudolph-Owen et al. method is for treating cancer; Rudolph-Owen et al. does not put the skilled person in possession of a method of hydrating skin or promoting skin desquamation

Claim 32 has been rejected under 35 U.S.C. §102(b) as being anticipated by van de Sandt et al. (In Vitro Cellular & Developmental Biology: Animal, 1995, 31(910): 761-766). Claim 32 has been cancelled and therefore rejection of this claim is moot. Further with respect to van de Sandt et al. and all of the present claims, a method for inducing cell proliferation using SDS does not inherently anticipate the present method for promoting desquamation of the skin and/or for promoting hydration of the skin as claimed herein. It is not correct to hold there is inherency.

Applicants' method does not use SDS alone but only in combination with specific hydrolase polypeptides as an activator thereof. Moreover, applicants' method is directed to desquamation and hydration, not cell proliferation. These are important distinctions which mean applicants' method is clearly not anticipated by van de Sandt et al. method.

Claim 32 has been rejected under 35 U.S.C. §102(b) as being anticipated by Martinez. (FR 2,357,246, with DERWENT English abstract) Claim 32 has been cancelled and therefore rejection of this claim is moot. Further with respect to Martinez and all of the present claims, a method for treating inflammation does not inherently anticipate the present method for promoting desquamation of the skin and/or for promoting hydration of the skin. It is not correct to hold there is inherency. In addition to the difference in the hydrolase polypeptide, the method is applied to a different population. The individual in need of skin desquamation or hydration of applicants' claims is a healthy person or one having a desquamation problem. The person treated by Martinez is suffering from inflammation. This is an important distinction which means applicants' method is clearly not anticipated by Martinez method. The fact that Martinez's composition is topical is irrelevant; Martinez does not put the skilled person in possession of a method of hydrating skin or promoting skin desquamation.

For at least the reasons set forth above, all of the claims now in the application are free of the record § 102 rejections.

35 U.S.C. §103(a) prior art rejections

Claims 1-11, 13, 14, 16, 17, 21, 24, 25, 27-29 and 32-42 have been rejected under 35 U.S.C. §103(a) as unpatentably obvious over Rudolph-Owen et al. in view

of Dalko et al. (US 2003/0113284), Collin et al. (US 5,667,789) and Herschler et al. (US 3,551,554).

Claims 2-8, 32 and 34 have been cancelled and therefore rejection of these claims are moot. Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29 and 32-42 remain in this application. Applicants respectfully submit these remaining claims are not obvious over Rudolph-Owen et al. in view of Dalko et al., Collin et al. and Herschler et al. and these claims are allowable.

To establish a *prima facie* case of obviousness, three basic criteria must be met. (MPEP 2143) First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Rudolph-Owen et al. teach that the expression of the 25943 gene is a polypeptide, referred to as "25943", that is a glycosylasparaginase. Rudolph-Owen et al. teach that 25943 can be used in the treatment of cellular proliferation disorders.

Dalko et al. teach the use of at least one DHEA derivative for improving the appearance of keratinous substances, such as the skin, hair, eyelashes and/or nails, in particular for preventing or treating cutaneous signs of ageing and/or a faded complexion and/or disorders of pigmentation of the skin or hair and/or drying of the skin and/or hyperseborrhoea and/or imperfections related to hyperseborrhoea and/or sensitive skin and/or dandruff and/or hair loss and/or canities.

Collin et al. discloses the use of salicylic acid derivatives as stabilizers for oil-in-water emulsions. Collin et al. teaches use of these emulsions for the treatment or care of skin, including preventing ageing and/or pigmentation of the skin.

Herschler et al. discloses compositions comprising DMSO for enhancing penetration of compounds through skin.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There is no suggestion or motivation in Rudolph-Owen et al. to use the any of the specific hydrolase polypeptides having amidase activity of the present claims to promote desquamation of the skin and/or promote hydration of the skin. Neither Dalko et al., Collin et al. or Herschler et al. suggest or provide motivation to use the specific hydrolase polypeptides having amidase activity required in the claims of the instant application. Rudolph-Owen et al. also does not suggest or provide motivation to use an activator of the specific hydrolase polypeptides having amidase activity required in the claims of the instant application. Neither Dalko et al., Collin et al. or Herschler et al. suggest or provide motivation to use an activator of the specific hydrolase polypeptides having amidase activity required in the claims of the instant application. Therefore, there is no suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to obtain the invention of the instant application.

To establish a *prima facie* case of obviousness, there must be a reasonable expectation of success. There is no reasonable expectation of success based on the teachings in Rudolph-Owen et al. to use the any of these specific hydrolase polypeptides having amidase activity to promote desquamation of the skin and/or promote hydration of the skin. The teachings of Rudolph-Owen et al. regard a

specific polypeptide that is a glycosylasparaginase which is not one of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Rudolph-Owen et al. are silent on the use of an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Rudolph-Owen et al. teach the use of a specific polypeptide that is a glycosylasparaginase for treatment of cellular proliferation disorders, such as cancers. Combining the teachings of Rudolph-Owen et al. with the teachings of Dalko et al., Collin et al. and Herschler et al. would not result in a reasonable expectation of success in arriving at the invention of the instant application. There is no reasonable expectation of success in using a compound with a different set of properties than a specific compound taught in the references, to treat a condition that was not taught or related to the treatment taught in those references.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Rudolph-Owen et al. teach the use of the expression of the 25943 gene that is a glycosylasparaginase. Rudolph-Owen et al. does not teach or suggest the use of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Neither Dalko et al., Collin et al. or Herschler et al. teach or suggest the use of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Rudolph-Owen et al. does not teach or suggest the use of an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Neither Dalko et al., Collin et al. or Herschler et al. teach or suggest the use of an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of

the instant application. Therefore, the prior art references, either alone or combined do not teach or suggest all the claim limitations.

Applicants respectfully submit that claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29 and 32-42 are not obvious over Rudolph-Owen et al. in view of Dalko et al., Collin et al. and Herschler et al. and that these claims are allowable.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25 and 27-29 (Group 1) are not obvious over by Rudolph-Owen et al. in view of Dalko et al., Collin et al. and Herschler et al. because (1) there is no suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there is not reasonable expectation of success; and (3) the prior art references do not teach or suggest all the claim limitations. None of the references teach or suggest applying (i) at least one hydrolase polypeptide having amidase activity, selected from the specific Markush group listed the current claims and (ii) at least one activator of the at least one hydrolase polypeptide.

Claims 33 and 35-42 (Group 2) are not obvious over Rudolph-Owen et al. in view of Dalko et al., Collin et al. and Herschler et al. because (1) there is no suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there is not reasonable expectation of success; and (3) the prior art references do not teach or suggest all the claim limitations. None of the references teach or suggest applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity, and (ii) at least one activator of aspartylglucosaminidase (AGA).

Claims 43-51 (Group 3) are not obvious over Rudolph-Owen et al. in view of Dalko et al., Collin et al. and Herschler et al. because (1) there is no suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there is not reasonable expectation of success; and (3) the prior art references do not teach or suggest all the claim limitations. None of the references teach or suggest applying (i) at least one hydrolase polypeptide having amidase activity, selected from the specific Markush group in the current claims and (ii) at least one activator of the at least one hydrolase polypeptide, where the activator is sodium dodecyl sulfate or sodium lauryl ether sulfate.

Claims 52-60 (Group 4) are not obvious over Rudolph-Owen et al. in view of Dalko et al., Collin et al. and Herschler et al. because (1) there is no suggestion or motivation either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there is not reasonable expectation of success; and (3) the prior art references do not teach or suggest all the claim limitations. None of the references teach or suggest applying (i) aspartylglucosaminidase (AGA) as the hydrolase polypeptide having amidase activity and (ii) the activator being sodium dodecyl sulfate or sodium lauryl ether sulfate.

Claims 1, 7-11, 13, 14, 16, 17, 24, 25, 27-29 and 32 have been rejected under 35 U.S.C. §103(a) as being obvious over Meyers in view of Dalko et al., Collin et al. and Herschler et al.

Claims 7, 8 and 32 have been cancelled and therefore rejection of these claims are moot. Claims 1, 9-11, 13, 14, 16, 17, 24, 25 and 27-29 remain in this application. Applicants respectfully submit these remaining claims are not obvious over Meyers in view of Dalko et al., Collin et al. and Herschler et al. and these claims are allowable.

Meyers teaches novel asparaginases, referred to as "26443" and "46873", that are nucleic acid and protein molecules that can be used in the treatment of cellular proliferation disorders.

The teachings of Dalko et al., Collin et al. and Herschler et al. were discussed above.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There is no suggestion or motivation in Meyers to use the any of the specific hydrolase polypeptides having amidase activity required in the instant claims to promote desquamation of the skin and/or promote hydration of the skin. Neither Dalko et al., Collin et al. or Herschler et al. suggest or provide motivation to use the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Meyers also does not suggest or provide motivation to use an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Neither Dalko et al., Collin et al. or Herschler et al. suggest or provide motivation to use an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Therefore, there is no suggestion or motivation, either in the cited references themselves or in the knowledge generally available to

one of ordinary skill in the art, to modify the reference or to combine reference teachings to obtain the invention of the instant application.

To establish a *prima facie* case of obviousness, there must be a reasonable expectation of success. There is no reasonable expectation of success based on the teachings in Meyers to use the any of these specific hydrolase polypeptides having amidase activity of applicants' claims to promote desquamation of the skin and/or promote hydration of the skin. The teachings of Meyers regard two specific novel asparaginases rather than the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Meyers is silent on the use of an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Meyers teach the use of two specific asparaginases in the treatment of cellular proliferation and/or differentiation disorders. Combining the teachings of Meyers with the teachings of Dalko et al., Collin et al. and Herschler et al. would not result in a reasonable expectation of success in arriving at the invention of the instant application. There is no reasonable expectation of success in using a compound with a different set of properties than a specific compound taught in the references, to treat a condition that was not taught or related to the treatment taught in those references.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Meyers teaches the use of the expression of two novel asparaginases. Meyers does not teach or suggest the use of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Neither Dalko et al., Collin et al. or Herschler et al. teach or suggest the use of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant

application. Meyers does not teach or suggest the use of an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Neither Dalko et al., Collin et al. or Herschler et al. teach or suggest the use of an activator of the specific hydrolase polypeptides having amidase activity as required in the claims of the instant application. Therefore, the prior art references, either alone or combined do not teach or suggest all the claim limitations.

Applicants respectfully submit that Claims 1, 9-11, 13, 14, 16, 17, 24, 25 and 27-29 are not obvious over Meyers in view of Dalko et al., Collin et al. and Herschler et al. and these claims are allowable. The other claims now in this application are allowable for at least the same reasons set forth above.

In view of the foregoing, it is believed that the record rejections cannot be maintained against the claims now in this application. Further, favorable action in the form of a Notice of Allowance is believed to be next in order and is earnestly solicited.

Respectfully submitted,

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